## AMENDMENTS TO THE SPECIFICATION

The specification has been amended in accordance with Examiner's suggestions with respect to the proper identification of trademarks.

Please amend the paragraph beginning at page 192, line 10, as follows:

The study involves administration of an intranasal effective amount of an exemplary formulation of the invention, Formulation F9 in the presence of a permeabilizing peptide, for example, JAM-1 NP-A peptide, occludin NP-26 peptide, and/or claudin-2 NP-27 peptide, as described above, to evaluate the absorption and tolerance of the interferon-β intranasal formulation by the subjects. See Tables 12 and 13. Formulations comprising permeabilizing peptides of JAM, occludin or claudin have a concentration range of permeabilizing peptide between approximately 0.1 mM and approximately 1.0 mM of JAM, occludin or claudin peptide in the formulation. The study is a single dose, parallel group pharmacokinetic/pharmacodynamic study to evaluate absorption and tolerance of interferon-β-1a by two routes of administration: intramuscular and intranasal. The objective of the study is to evaluate the absorption, tolerance and pharmacodynamic parameters of equimolar doses of an exemplary formulation of interferon-β-1a in combination with one or more intranasal delivery-enhancing agents of the present invention, for example, permeabilizing peptides of JAM, occludin or claudin, administered intranasally, versus interferon-β-1a (~~Avonex®~~ AVONEX® (Interferon beta-1a), Biogen, Inc., or ~~Rebif®~~ REBIF® (Interferon beta-1a), Serono) administered intramuscularly, subcutaneously, or in the presence or absence of one or more intranasal delivery-enhancing agents.

Please amend the paragraph beginning at page 193, line 14, as follows:

**Protocol:** 36 healthy male subjects, age 18-50, are generally enrolled in the study. Groups of six subjects typically receive either Formulation F9 (60 μg; 6.0 MIU; interferon-β-1a), Formulation JAM-1 NP-A ( = F9 + 1.0 mM JAM-1 NP-A peptide); Formulation CLAUDIN-2 NP-27 ( = F9 + 1.0 mM CLAUDIN-2 NP-27 peptide); or Formulation OCCLUDIN NP-26 ( = F9 + 1.0 mM OCCLUDIN NP-26 peptide) delivered intranasally as two 0.1 mL sprays, each containing 30 μg/0.1 mL. Six subjects receive a single dose of 60 μg interferon-β-1a (~~Avonex®~~ AVONEX® (Interferon beta-1a)) delivered intramuscularly. Six subjects receive a single dose of 60 μg interferon-β-1a (~~Rebif®~~ REBIF® (Interferon beta-1a); Ares-Serono) delivered subcutaneously.

Please amend the paragraph beginning at page 194, line 4, as follows:

In accordance with the foregoing teachings Table 14, below, provides projected exemplary pharmacokinetic data for intranasal delivery of interferon-β-1a in a pharmaceutical formulation of the invention (e.g., Formulation F-9 plus permeabilizing peptides of JAM-1, claudin-2, or occludin) compared to Formulation F-9 without permeabilizing peptide, intramuscular, or subcutaneous delivery of interferon-β-1a ~~(Avonex® or Rebif®)~~ (AVONEX® (Interferon beta-1a) or REBIF® (Interferon beta-1a)). Maximum concentration of interferon-β in the blood serum ($C_{max}$) at 3 hours post dosing is projected to be approximately 6.0 IU/mL for intranasal delivery of JAM-1 NP-A Formulation; 5.6 IU/mL for intranasal delivery of Claudin-2 NP-27 Formulation, 4.5 IU/mL for intranasal delivery of Occludin NP-26 Formulation--compared to 5.1 IU/mL for subcutaneous delivery of interferon-β-1a (at 12 MIU dose) or 4.9 to 5.2 IU/mL for intramuscular delivery of interferon-β-1a (at 12 MIU dose).

Please amend the paragraph beginning at page 194, line 16, as follows:

Time to maximum serum concentration of interferon-β in the blood serum ($t_{max}$) is projected to be at least 5- to 10-fold faster for intranasal delivery of the formulation of the present invention compared to subcutaneous or intramuscular delivery of interferon-β-1a ~~(Avonex® or Rebif®)~~ (AVONEX® (Interferon beta-1a) or REBIF® (Interferon beta-1a)). In exemplary embodiments $t_{max}$ for intranasal delivery of JAM-1 NP-A Formulation is projected to be approximately 0.3 hours, or 0.3 hours for intranasal delivery of Claudin-2 NP-27 Formulation, or 0.4 hours for intranasal delivery of Occludin NP-26 Formulation--compared to a $t_{max}$ of 3 to 4 hours for intramuscular or subcutaneous administration of ~~(Avonex® or Rebif®)~~ (AVONEX® (Interferon beta-1a) or REBIF® (Interferon beta-1a)).

Please replace the Table 14 beginning at page 196, line 1 with the following Table 14:

**TABLE 14: Pharmacokinetic and pharmacodynamic parameters[a]**

| | REBIF®, Interferon beta-1a, SC 12 MIU (60 µg) dose | REBIF®, Interferon beta-1a, IM 12 MIU (60 µg) dose | AVONEX®, Interferon beta-1a IM 12 MIU (60 µg) dose | Intranasal Formulation F9 12 MIU (60 µg) dose | Intranasal Formulation JAM-1 NP-A + F9 (12 MIU) dose | Intranasal Formulation CLAUDIN2 NP-27 + F9 (12 MIU) dose | Intranasal Formulation OCCLUDIN NP-26 + F9 (12 MIU) dose |
|---|---|---|---|---|---|---|---|
| **Serum IFN-$\beta$:** | | | | | | | |
| $AUC_{0\text{-}24h}$ (IU h/ml) | 65 | 70 | 65 | 70 | 85 | 78 | 75 |
| $C_{max}$ (IU/ml) | 5.1 | 5.2 | 4.9 | 4.4 | 6.0 | 5.6 | 4.5 |
| $t_{max}$ (h) | 3 | 3.5 | 4 | 0.4 | 0.3 | 0.3 | 0.4 |
| **Serum neopterin:** | | | | | | | |
| $AUC_{0\text{-}144h}$ (nmol h/l) | 2700 | 2930 | 2974 | 195.5 (0-96h) ng•h/ml | 263 (0-96h) ng•h/ml | 243 (0-96h) ng•h/ml | 196 (0-96h) ng•h/ml |
| $C_{max}$ (nmol/l) | 32 | 35 | 36 | 2.82 ng/ml | 3.86 ng/ml | 3.54 ng/ml | 2.90 ng/ml |
| $t_{max}$ (h) | 36 | 36 | 36 | 23.9 | 19.1 | 19.1 | 23.9 |
| **Serum $\beta_2$-microglobulin:** | | | | | | | |
| $AUC_{0\text{-}24h}$ (mg h/l) | 271 | 277 | 270 | 238 (0-96h) µIU•h/ml | 329 (0-96h) µIU•h/ml | 305 (0-96h) µIU•h/ml | 246 (0-96h) µIU•h/ml |
| $C_{max}$ (mg/l) | 2.3 | 2.4 | 2.3 | 2.1 □g/ml | 2.8 □g/ml | 2.6 □g/ml | 2.1 □g/ml |
| $t_{max}$ (h) | 24 | 36 | 36 | 35.3 | 26.5 | 30.9 | 34.3 |

[a]Per hour and $10^4$ cells.
*$P$= 0.015, AVONEX® (Interferon beta-1a) IM > REBIF® (Interferon beta-1a) SC

Data on AVONEX® (Interferon beta-1a) and REBIF® (Interferon beta-1a): Munafo, et al., Eur. J. Neurology, 5: 187-193, 1998, .

Please amend the paragraph beginning at page 197, line 1, as follows:

In accordance with the foregoing teachings Table 14, below, provides projected exemplary pharmacokinetic for intranasal delivery of interferon-β-1a in a pharmaceutical formulation of the present invention (e.g., Formulation F-9 plus permeabilizing peptides of JAM-1, claudin-2, or occludin) compared to subcutaneous or intramuscular delivery of interferon-β-1a ~~(Avonex® or Rebif®)~~ (AVONEX® (Interferon beta-1a) or REBIF® (Interferon beta-1a)) or intranasal adminstration of Formulation F-9. The projected results in Table 15 compare simultaneous intranasal delivery of interferon-β-1a and permeabilizing peptides, JAM-1, claudin-2, or occludin, compared to intranasal delivery of permeabilizing peptides, JAM-1, claudin-2, or occludin preceding intranasal delivery of interferon-β-1a by 10, 20 or 30 minutes.

Please amend the paragraph beginning at page 197, line 21, as follows:

Time to maximum serum concentration of interferon-β in the blood serum ($t_{max}$) is projected to be approximately 0.3 hours for intranasal delivery of Formulation F-9 (IFN-β-1a) plus permeabilizing peptide JAM-1 NP-A administered simultaneously. $t_{max}$ is projected to be approximately 0.25 hours for intranasal delivery of permeabilizing peptide JAM-1 NP-A preceding by 10 minutes intranasal delivery of Formulation F-9, or approximately 0.2 hours for intranasal delivery of permeabilizing peptide JAM-1 NP-A preceding by 20 minutes or 30 minutes intranasal delivery of Formulation F-9. These values compare to a $t_{max}$ of 3 to 4 hours for intramuscular or subcutaneous administration of ~~(Avonex® or Rebif®)~~ (AVONEX® (Interferon beta-1a) or REBIF® (Interferon beta-1a)).